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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/531,438	GIBERT ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-73 and 80-91* is/are pending in the application.

4a) Of the above claim(s) *90 and 91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-73 and 80-89* is/are rejected.

7)☒ Claim(s) *42-44,81,83,85 and 89* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 42-73,80-91 are pending.
Claims 42-73 and 80-89 are under consideration
Claims 90-91 stand withdrawn from consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections/Rejections Maintained

2. Claims 60, 81,83,85,87 and 89 rejected under 35 U.S.C. 112, first paragraph (scope) made of record in the last office is herein maintained for reasons of record.

3. In light of the newly amended claim limitations submitted "the all of the complementary strand", which is unclear the following prior art rejections are being maintained as the claims still read on Applicant's definitions at pages 4 and 5 of the instant Specification that include portions, fragments and variants of the recited SEQ ID Nos, and nucleic acid molecules that comprise these fragments and portions and also meet the recited functional limitations. See rejection under 35 USC 112, second paragraph below.

4. Claims 60,81,83,85,87 and 89 rejected under 35 U.S.C. 102(b) as being anticipated by Hunter et al, for reasons of record, and responses set forth below.

5. Claims 43, 44 and 42, subparagraph (a), 60 SEQ ID N0 4, and claims 80,82;84,86 and 88

6. (paragraph a) comprise subject matter that defnes over the prior art of record ~~(see paragraphs 7-10, paper number 23) but are objected to as reciting a rejected embodiment or dependent upon a rejected base claim, but would be allowable upon obviation of the objection.~~

Response to Arguments

7. Claims 60, 81,83,85,87 and 89 rejected under 35 U.S.C. 112, first paragraph (scope) is traversed on the grounds that:

a. The claims have been amended to recite specific stringent conditions which hybridize;

b. And to recite the "central structural features", specifically a hydrophobic region bordered by a charged amino acids.

8. It is the position of the examiner that the claims recite the washing conditions and not the hybridization conditions. Applicant's traversal is not commensurate in scope with the instantly claimed invention (see New Matter rejection below). While the hybridization **process** may comprise a step of washing, the hybridization conditions are not the washing step conditions.

7. Additionally, the claims do not recite the combination of claim limitations "central structural features" used to traverse the scope of enablement rejection. The scope of enablement rejection is maintained for reasons of record.

8. The rejection of claims 60,81,83,85,87 and 89 under 35 U.S.C. 102(b) as being anticipated by Hunter et al , is traversed on the grounds that the disclosed sequence of Hunter et al:

c. Does not describe a sequence from a Clostridium strain;

d. Which will hybridize to SEQ ID NO 4; and

e. Encodes a peptide that functions as a secretion signal peptide that

f. Comprises a hydrophobic region bordered by charged amino acids.

9. It is the position of the examiner that Hunter et al:

g. do disclose and describe a Clostridium perfringens nucleic acid that is within the definition of "nucleic acid" of the instant specification at page 4 includes portions and fragments of the nucleic acid of SEQ ID No 4. The nucleic acid Hunter et al comprises a sequence that encodes a secretion signal peptide for a Clostridium perfringens protein. Hunter at Figure 2, page 3961, discloses this embodiment.

h. The disclosed "purified nucleic acid" of Hunter et al comprises "a sequence which will hybridize to SEQ ID NO 4 (the complement of SEQ ID NO 4), specifically "ATGAAGAAA" (encodes MKK), the disclosed nucleic acid sequence comprising a sequence encoding a secretion signal peptide.

i. Additionally, the recombinant DNA, of Hunter et al, hybridized with Clostridium perfringens Type C toxin. The Instant Specification isolated the

Clostridium perfringens beta toxin nucleic acid , of the preferred embodiment, from a type-C strain. Hunter et al showed their purified nucleic acid to be able to hybridize to a type-C strain nucleic acid (see Hunter et al, Figure 6, row B, lane B1

i. The purified nucleic acid of Hunter et al comprises a nucleic sequence "MKK" that will hybridize to SEQ ID NO 4 and also

j. comprises a hydrophobic region: "Phe Ile ser Val Ile Val ser ser Leu Leu Met gly cys Leu Leu ser Phe thr Leu Val tyr Ala asn" (all amino acids with a capital first letter (14 of 22 amino acids) (The disclosed hydrophobic region of Hunter et al therefore meets the recited claim limitations for the nucleic acid that " encodes a peptide comprising a hydrophobic region"),

k. wherein the hydrophobic region is "bordered by charged amino acids" specifically "Lys Lys Lys" at the N' terminal side of the region (which are all positively charged amino acids at positions 2-4, Hunter et al sequence page 3961, amino acid sequence below coding nucleic acid sequence), and Aspartic Acid at the C' terminal side, at position 29, a negative charged amino acid (see Hunter et al, Figure 2, amino acid sequence) .

10. The rejection of claims 42(b) and claims 50-51,54-55(b) rejected under 35 U.S.C. 102(b) as being anticipated by Graves et al (1986) is traversed on the grounds that "Graves et al do not describe the purified nucleic acid as claimed in the amended claim 42(b) submitted herein, i.e., hybridizing under stringent conditions to all of the complementary strand of SEQ ID NO 3".

11. It is the position of the examiner that the newly amended claims recite the phrase "hybridizing the all of the complementary strand", which is a different phrase than that used to traverse the reference applied against the claims. Amendment of the claims to recite -----over the full length of the complementary strand---- could obviate this rejection. This rejection is maintained in light of the new grounds of rejection under 35 USC 112, second paragraph introduced by the submitted claim amendment.

12. The rejection of claims 42(b), 45-73, 81,83,85,87 and 89(b) rejected under 35 U.S.C. 102(b) as being anticipated by Brown et al is traversed on the grounds that the abstract does not describe what type of secretory leader sequence was used and particularly does not describe the secretory leader sequence is of a Clostridium strain.

13. The examiner is providing herewith the entire dissertation document that is over 200 pages in length which shows the secretory leader sequence to be obtained from a Clostridium strain (see Figure 51, clostripain leader, defined to be the secretion leader sequence of Dargatz et al (1993) deposited in EMBL (Feb 1992) accession number X63673 and under Swiss-Prot accession number P09870, the first 27 amino acids).

14. The promoter is a Clostridial ferrodoxin promoter as described in Table 3 (nucleic acid sequence provided, along with additional Clostridium promoter nucleic acid sequences)).

15. Also see narrative of 6.3.2 for the Clostridial nucleic acid components contained in the recombinant expression vector cassette. The rejection is maintained for reasons of record and responses set forth herein.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

16. Claims 60, and 80-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

17. Claims 60 and 80-89 recite the phrase "a sequence which hybridizes under stringent conditions to SEQ ID NO:4, wherein the stringent conditions comprise washing". The examiner upon consideration of the definitions and disclosure provided by the Instant Specification could not find original descriptive support for the hybridization conditions to be washing conditions. At page 5, lines 4-17, the term "hybridizing" was defined to be different conditions from the wash. The conditions for hybridization are differently defined from that of the wash (see semi-colon separating the defined conditions). The combination of claim limitations set forth in claims 60 and 80-89 which define the hybridization to be the washing conditions does not evidence original descriptive support in the instant Specification, and therefore recite New Matter.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. The term "stringent conditions" in all of the claims (claims 42-73, 80-89) is a relative term which renders the claim indefinite. The term "stringent conditions" for incubating the hybridization reaction is not defined by the claim, the specification does not provide a standard

for ascertaining the requisite degree, as the Specification at page 5, paragraph 2, states the conditions may be an "normal conditions". One of ordinary skill in the art would not be reasonably appraised of the scope of the invention, and what the nucleic acid is based upon the recitation of a relative term which in turn is defined by a relative term "normal", as the resultant structure is not defined absent a clear definition of the conditions used to produce the claimed product. This rejection could be obviated through amendment of the independent claims to recite the phrase ----- 42 degrees C, 50% formamide, 5X SSC and 1X Denhardt ------(support found on page 5, paragraph 2, lines 6-7).

20. Claim 42-59,61-73 are rejected under 35 USC 112, second paragraph. The claims have been amended to recite the phrase: " hybridizing the all of the complementary strand". The meaning of this phrase is unclear. What is the "all"? The term "all" lacks antecedent basis in the claims.

Conclusion

1. This is a non-final action.

1. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

2. Bullifent, HL et al (1995) is cited to show a Clostridium perfringens reporter system.

3. Matsushita et al (1996) is cited to show a Clostridium perfringens promoter.

4. Melville, SB et al (1994) is cited to show a Clostridium perfringens promoter (see title)

5. Pickett et al (June 1996) is cited to show a Campylobacter jejuni peptide sequence that shares 64% identity over 9 of the first 14 amino acids of the peptide encoded by SEQ ID NO 4 (see attached alignment).

6. Song, K (1995, abstract) is cited to show a Clostridium difficile promoter.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
February 15, 2005

MARK NAVARRO
PRIMARY EXAMINER